

FORM PTO-1300 (REV 11-90)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER 788-027	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				U.S. APPLICATION NO. (If known, see 37 CFR 1.5)	
INTERNATIONAL APPLICATION NO. PCT/EP99/06056		INTERNATIONAL FILING DATE 18 August 1999		PRIORITY DATE CLAIMED 20 August 1998	
TITLE OF INVENTION SYNERGISTIC BIOCIDE COMPOSITION					
APPLICANT(S) FOR DO/EO/US Dagmar ANTONI-ZIMMERMANN; Rudiger BAUM; Thomas WUNDER; and Hans-Jurgen SCHMIDT					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
<ol style="list-style-type: none"> <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> a. <input checked="" type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)). <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> a. <input checked="" type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> have been transmitted by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 					
Items 11. to 16. below concern document(s) or information included:					
<ol style="list-style-type: none"> <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. <input checked="" type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. <input type="checkbox"/> A substitute specification. <input type="checkbox"/> A change of power of attorney and/or address letter. <input checked="" type="checkbox"/> Other items or information: PCT publication with Int'l. Search Report; English Translation of letter to WIPO with amended claim 1 Form PTO-1449 					
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U.S. APPLICATION NUMBER / PCT NUMBER 09/509932		INTERNATIONAL APPLICATION NO PCT/EP99/06056	ATTORNEYS DOCKET NUMBER 788-027																				
17. <input checked="" type="checkbox"/> The following fees are submitted:		CALCULATIONS PTO USE ONLY																					
<p>BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5) :</p> <p>Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$970.00</p> <p>International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$840.00</p> <p>International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$760.00</p> <p>International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$670.00</p> <p>International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) \$96.00</p>																							
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<p>Surcharge of \$130.00 for furnishing the oath or declaration later than <input checked="" type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th>CLAIMS</th> <th>NUMBER FILED</th> <th>NUMBER EXTRA</th> <th>RATE</th> </tr> <tr> <td>Total claims</td> <td>8 - 20 =</td> <td>0</td> <td>X \$18.00</td> </tr> <tr> <td>Independent claims</td> <td>1 - 3 =</td> <td>0</td> <td>X \$78.00</td> </tr> <tr> <td colspan="2">MULTIPLE DEPENDENT CLAIM(S) (if applicable)</td> <td>0</td> <td>+\$260.00</td> </tr> <tr> <td colspan="4" style="text-align: right;">TOTAL OF ABOVE CALCULATIONS = <input type="text" value="970.00"/></td> </tr> </table>				CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	Total claims	8 - 20 =	0	X \$18.00	Independent claims	1 - 3 =	0	X \$78.00	MULTIPLE DEPENDENT CLAIM(S) (if applicable)		0	+\$260.00	TOTAL OF ABOVE CALCULATIONS = <input type="text" value="970.00"/>			
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TOTAL OF ABOVE CALCULATIONS = <input type="text" value="970.00"/>																							
<p>Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: right;">SUBTOTAL =</td> <td><input type="text" value="970.00"/></td> </tr> <tr> <td colspan="2">Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).</td> </tr> <tr> <td colspan="2" style="text-align: right;">TOTAL NATIONAL FEE = <input type="text" value="970.00"/></td> </tr> <tr> <td colspan="2">Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property</td> </tr> <tr> <td colspan="2" style="text-align: right;">TOTAL FEES ENCLOSED = <input type="text" value="970.00"/></td> </tr> <tr> <td colspan="2"></td> <td style="text-align: right;">Amount to be: <input checked="" type="checkbox"/> refunded <input type="checkbox"/> charged</td> <td style="text-align: right;">\$ \$</td> </tr> </table>				SUBTOTAL =	<input type="text" value="970.00"/>	Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).		TOTAL NATIONAL FEE = <input type="text" value="970.00"/>		Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property		TOTAL FEES ENCLOSED = <input type="text" value="970.00"/>				Amount to be: <input checked="" type="checkbox"/> refunded <input type="checkbox"/> charged	\$ \$						
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<p>a. <input checked="" type="checkbox"/> A check in the amount of <input type="text" value="970.00"/> to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>08-1540</u>. A duplicate copy of this sheet is enclosed.</p>																							
<p>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.</p>																							
SEND ALL CORRESPONDENCE TO JAMES V. COSTIGAN, ESQ. HEDMAN, GIBSON & COSTIGAN, P.C. 1185 AVENUE OF THE AMERICAS, SUITE 2003 NEW YORK, NY 10036-2646 212-302-8989		 SIGNATURE JAMES V. COSTIGAN NAME <input type="text" value="25,669"/> REGISTRATION NUMBER																					

09/509932
527 Rec'd PCT/PTO 03 APR 2000

Docket No.: 788-027

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT OPERATIONS

In re Application of:)
Dagmar ANTONI-ZIMMERMANN) Group Art Unit: --
Rüdiger BAUM)
Thomas WUNDER) Examiner: --
Hans-Jürgen SCHMIDT)
Serial No.: Not Yet Assigned)
Filed: Concurrently Herewith)
For: SYNERGISTIC BIOCIDE COMPOSITION

New York, NY 10036
April 3, 2000

Box PCT
Assistant Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

SIR:

Kindly amend claim 1 by deleting the bracketed subject matter and inserting the underlined material:

1. (amended) Biocide composition as an additive to substances susceptible to infestation by harmful organisms, containing 2-methylisothiazolin-3-one as a biocidal agent, characterized in that the biocide composition contains 3-iodo-2-propynyl-N-butylicarbamate as a further biocidal agent, with the exception of biocide compositions containing 5-chloro-2-methylisothiazolin-3-one.

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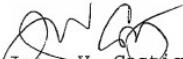
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Assistant Commissioner for Patents
Washington, DC 20231
James V. Costigan, Registration No. 25,669
~~(Indicates name of person mailing)~~

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REMARKS

This Amendment is being filed to conform the text of claim 1 to claim 1 as amended during the PCT examination.

Respectfully submitted,


James V. Costigan
Registration No. 25,669

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SEARCHED - INDEXED - SERIALIZED - FILED

Translation of PCT application as filed

1

Description

The invention relates to a biocide composition as an additive to substances susceptible to infestation by harmful organisms. In particular, the invention relates to a
5 biocide composition containing 2-methylisothiazolin-3-one as a biocidal agent.

Biocidal agents are used in many areas, for example, to combat harmful bacteria, fungi, or algae. It has been known for a long time to use 4-isothiazolin-3-ones (also known as 3-isothiazolones), since these include very effective biocidal compounds.

10

One of those compounds is 5-chloro-2-methylisothiazolin-3-one. While it has a good biocidal effect, it also has various disadvantages during practical use. For example, the compound frequently triggers allergies in people who handle it. In addition, in some countries there are legal limitations for the AOX value, i.e., a specific concentration in water of organic chlorine, bromine, and iodine compounds that are absorbable by activated charcoal may not be exceeded. That then prevents the use of 5-chloro-2-methylisothiazolin-3-one to the desired extent. Moreover, the stability of that compound is insufficient under certain conditions, e.g., at high pH values or in the presence of nucleophiles or reducing agents.

20

Another known isothiazolin-3-one with a biocidal effect is 2-methylisothiazolin-3-one. While the compound does avoid various disadvantages of 5-chloro-2-methylisothiazolin-3-one, for example, the high allergy risk, it also has a much lower biocidal effect. Simply replacing 5-chloro-2-methylisothiazolin-3-one with 25 2-methylisothiazolin-3-one is therefore not possible.

30

It is also known to use a combination of various isothiazolin-3-ones. For example, a synergistic biocide composition is described in EP 0676140 A1 that contains 2-methylisothiazolin-3-one (2-methyl-3-isothiazolone) and 2-n-octylisothiazolin-3-one (2-n-octyl-3-isothiazolone).

RECORDED - RECEIVED -

In JP 01224306 (Chemical Abstracts, volume 112, no. 11, March 12, 1990, abstract no. 93924), a biocide composition is described that is made of 2-methylisothiazolin-3-one, 1,2-benzisothiazolin-3-one, and 5-chloro-2-methylisothiazolin-3-one.

5

From US 5328926, synergistic biocide compositions are known that are combinations of 1,2-benzisothiazolin-3-one and an iodopropargyl compound (iodopropynyl compound). As such a compound, 3-iodopropargyl-N-butylcarbamate is mentioned.

10

The object of the invention is to provide a biocide composition that is improved in that its components synergistically cooperate and therefore can be used with simultaneous deployment in lower concentrations compared to the necessary concentrations in the case of individual components. In that way, humans and the environment are to be less polluted and the costs of combating harmful microorganisms are to be reduced.

15

The object is attained according to the invention by a biocide composition containing 2-methylisothiazolin-3-one as a biocidal agent, which is characterized in that it contains, as a further biocidal agent, 3-iodo-2-propynyl-N-butylcarbamate.

20

The biocide composition according to the invention has the advantage that it can replace active ingredients that have previously been used in practice but that have disadvantages with regard to health and the environment, such as 5-chloro-2-methylisothiazolin-3-one.

25

Moreover, the biocide compositions according to the invention can be produced, if necessary, using only water as a liquid medium. In that regard, the addition of emulsifiers, organic solvents, and/or stabilizers is not necessary.

30

The biocide composition according to the invention contains

2-methylisothiazolin-3-one and the 3-iodo-2-propynyl-N-butylcarbamate normally in the weight ratio of (100-1) : (1-50), preferably in the weight ratio of (15-1) : (1-8), in particular in the weight ratio of (4-1) : (1-4).

5 In the biocide composition, 2-methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate are present in a total concentration of preferably 0.5 to 50% by weight, in particular from 1 to 20% by weight, particularly preferably from 2.5 to 10% by weight, in each case based on the total biocide composition.

10 It is useful to use the biocides of the composition according to the invention in combination with a polar or nonpolar liquid medium. In that regard, that medium can be, for example, already present in the biocide composition and/or in the material to be preserved.

15 Preferable polar liquid media are water, an aliphatic alcohol having 1 to 4 carbon atoms, e.g., ethanol and isopropanol, a glycol, e.g., ethylene glycol, diethylene glycol, 1,2-propylene glycol, dipropylene glycol, and tripropylene glycol, a glycol ether, e.g., ethylene glycol monobutyl ether and diethylene glycol monobutyl ether, a glycol ester, e.g., butyl diglycol acetate, 2,2,4-trimethylpentanediolmonoisobutyrate, a polyethylene glycol, a polypropylene glycol, N,N-dimethylformamide, or a mixture of such substances. The polar liquid medium is in particular water, with the corresponding biocide composition preferably being neutral in its pH value, e.g., adjusted to a pH value of 6 to 8.

25 As a nonpolar liquid medium, aromatics, preferably xylene and toluene, are used.

The biocide composition according to the invention can also simultaneously be combined with a polar and a nonpolar liquid medium.

30 The biocide composition according to the invention can also contain one or more additional biocidal ingredients, which are selected as a function of the area of application.

Special examples of such additional biocidal agents are listed below.

- | | |
|----|--|
| | Benzyl alcohol |
| | 2,4-dichlorobenzyl alcohol |
| 5 | 2-phenoxyethanol |
| | 2-phenoxyethanol hemiformal |
| | Phenylethyl alcohol |
| | 5-bromo-5-nitro-1,3-dioxane |
| | Formaldehyde and formaldehyde releasing substances |
| 10 | Dimethylol dimethylhydantoin |
| | Glyoxal |
| | Glutaraldehyde |
| | Sorbic acid |
| | Benzzoic acid |
| 15 | Salicylic acid |
| | P-hydroxybenzoic acid ester |
| | Chloroacetamide |
| | N-methylochloroacetamide |
| | Phenols such as p-chloro-m-cresol and o-phenylphenol |
| 20 | N-methyloxurea |
| | N,N'-dimethyloxurea |
| | Benzyl formal |
| | 4,4-dimethyl-1,3-oxazolidine |
| | 1,3,5-hexahydrotriazine |
| 25 | Quaternary ammonium compounds, such as |
| | N-alkyl-N,N-dimethylbenzyl ammonium chloride and |
| | di-n-decyldimethyl ammonium chloride |
| | Cetyl pyridinium chloride |
| | Diguanidin |
| 30 | Polybiguanide |
| | Chlorhexidine |

- 1,2-dibromo-2,4-dicyanobutane
 3,5-dichloro-4-hydroxybenzaldehyde
 Ethylene glycol hemiformal
 Tetra-(hydroxymethyl)-phosphonium salts
 5 Dichlorophene
 2,2-dibromo-3-nitrilopropionic acid amide
 Methyl-N-benzimidazole-2-ylcarbamate
 2-n-octylisothiazolin-3-one
 4,5-dichloro-2-n-octylisothiazolin-3-one
 10 4,5-trimethylene-2-methylisothiazolin-3-one
 2,2'-dithio-dibenzoic acid-di-N-methylamide
 Benzisothiazolinone derivatives
 2-thiocyanomethylthiobenzothiazole
 C-formals, such as
 15 2-hydroxymethyl-2-nitro-1,3-propandiol
 2-bromo-2-nitropropane-1,3-diol
 Reaction products of allantoin

- Examples of the formaldehyde retardant substances are
 20 N-formals such as
 N,N'-dimethylurea
 N-methylurea
 Dimethylol dimethylhydantoin
 N-methylol chloroacetamide
 25 Reaction products of allantoin
 Glycol formals, such as
 Ethylene glycol formal
 Diethylene glycol monobutyl ether formal
 Benzyl formal
 30

The biocide composition according to the invention can contain other common ingredients that are known to those skilled in the art in the area of biocides. They are, for example, thickeners, anti-foaming agents, substances for adjusting pH value, aromas, dispersion aids, and coloring agents.

5

2-Methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate are known substances. 2-Methylisothiazolin-3-one can be prepared, for example, according to US 5466818. The reaction product thus obtained can be purified using, for example, column chromatography. The reaction product obtained when that is done can be purified using,

10

for example, column chromatography.

3-Iodo-2-propynyl-N-butylcarbamate is commercially available, for instance, from Troy Chemical Company under the trade names Polyphase®, Polyphase® AF-1, and Polyphase® NP-1 or from Olin Corporation under the trade name Omacide® IPBC

15

100.

The biocide composition according to the invention is a system in which the combination of 2-methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate synergistically develops a biocidal effect that is greater than that possessed by each of those compounds alone.

20

The biocide composition according to the invention can be used in very different areas. It is suitable, for example, for use in paints, plasters, lignin sulfonates, whitewashes, adhesives, photochemicals, products containing casein, products containing starch, asphalt emulsions, surfactant solutions, fuels, cleaning agents, cosmetic products, water systems, polymer dispersions, and cold lubricants for protecting against infestation, for example, by bacteria, filamentous fungi, yeasts, and algae.

25

In practical application, the biocide composition can either be applied as a ready-made mixture or by separately adding the biocides and the other components of the composition to the substance to be preserved.

30

C O P Y R I G H T
U S P T O W N
P R I V A T E
U S E
O N L Y

The Examples explain the invention.

Example 1

5 This Example demonstrates the synergy of combinations of 2-methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate in the biocide composition according to the invention.

10 For that purpose, aqueous mixtures with different concentrations of 2-methylisothiazolin-3-one (MIT) and 3-iodo-2-propynyl-N-butylcarbamate (IPBC) were produced and the effects of those mixtures on *Saccharomyces cerevisiae* were tested.

15 In addition to the biocide components and water, the aqueous mixtures also contained a nutrient medium, specifically a Sabouraud maltose broth (trade product "Merck No. 10393"). The cell density of *Saccharomyces cerevisiae* was 10^6 cells/ml. The incubation time was 72 hours at 25° C. Each sample was incubated at 120 r.p.m. on an incubation shaker.

20 Table I below provides the concentrations of MIT and IPBC that were used. It also shows whether growth of the microorganism occurred ("+" symbol) or not ("-" symbol).

25 Table I therefore also shows the minimal inhibitory concentration (MIC). Accordingly, with the use of MIT alone the result was an MIC value of 150 ppm and with the use of IPBC alone the result was an MIC value of 10 ppm. In contrast, the MIC values of mixtures of MIT and IPBC are clearly lower; in other words, MIT and IPBC have a synergistic effect in combination.

Table I

30 MIC values for *Saccharomyces cerevisiae*
 at an incubation time of 72 hours

MIT Concen- tration (ppm)	IPBC concentration (ppm)											
	15	12.5	10	7.5	5	4	3	2	1	0.5	0	
300	-	-	-	-	-	-	-	-	-	-	-	
250	-	-	-	-	-	-	-	-	-	-	-	
200	-	-	-	-	-	-	-	-	-	-	-	
150	-	-	-	-	-	-	-	-	-	-	-	
100	-	-	-	-	-	-	-	-	+	+	+	
75	-	-	-	-	-	-	+	+	+	+	+	
50	-	-	-	-	+	+	+	+	+	+	+	
25	-	-	-	-	+	+	+	+	+	+	+	
15	-	-	-	-	+	+	+	+	+	+	+	
10	-	-	-	-	+	+	+	+	+	+	+	
5	-	-	-	-	+	+	+	+	+	+	+	
0	-	-	-	+	+	+	+	+	+	+	+	

The synergy that occurs is shown in numerical terms based on the calculation of the synergy index shown in Table II. The calculation of the synergy index is performed according to the method by F. C. Kull et al., Applied Microbiology, vol. 9 (1961), p. 538. The synergy index is calculated here using the following formula:

25

$$\text{Synergy index SI} = Q_a/Q_A + Q_b/Q_B.$$

When this formula is used for the biocide system tested here, the variables in the formula have the following meaning:

30

- Q_a = Concentration of MIT in biocide mixture of MIT and IPBC
- Q_A = Concentration of MIT as the only biocide
- Q_b = Concentration of IPBC in biocide mixture of MIT and IPBC
- Q_B = Concentration of IPBC as the only biocide

35

When the synergy index shows a value greater than 1, that means that an

antagonism is present. When the synergy index has a value of 1, that means there was an addition of the effect of both biocides. When the synergy index has a value of less than 1, that means that a synergy of the two biocides exists.

Table II
Calculation of the synergy index for *Saccharomyces cerevisiae* at an incubation time of 72 hours

	MIC at		Total concentration MIT + IPBC $Q_a + Q_b$ (ppm)	Concentration		Q_a/Q_A	Q_b/Q_B	Synergy index $Q_a/Q_A + Q_b/Q_B$
	MIT concentration Q_a (ppm)	IPBC concentration Q_b (ppm)		MIT (% wt)	IPBC (% wt)			
0	10	10	0.0	100.0	0.00	1.00		1.00
5	7.5	12.5	40.0	60.0	0.03	0.75		0.78
10	7.5	17.5	57.1	42.9	0.07	0.75		0.82
25	5	30	83.3	16.7	0.17	0.50		0.67
50	5	55	90.9	9.1	0.33	0.50		0.83
75	4	79	94.9	5.1	0.50	0.40		0.90
100	2	102	98.0	2.0	0.67	0.20		0.87
150	0	150	100.0	0.0	1.00	0.00		1.00

Table II shows that the optimum synergy, e.g., the lowest synergy index (0.67) of an MIT/IPBC mixture, was at a mixture of 83.3% by weight MIT and 16.7% by weight IPBC.

25

Example 2

Example 1 was repeated with the change that the incubation time was 96 hours instead of 72 hours.

30

Table III below shows the MIC values of the tested biocide compositions. The MIC value with the use of MIT alone was 150 ppm and with the use of IPBC alone 10 ppm.

Table III

MIC values for *Saccharomyces cerevisiae*
at an incubation time of 96 hours

5	MIT Concen- tra-tion (ppm)	IPBC concentration (ppm)										
		15	12.5	10	7.5	5	4	3	2	1	0.5	0
10	300	-	-	-	-	-	-	-	-	-	-	-
	250	-	-	-	-	-	-	-	-	-	-	-
	200	-	-	-	-	-	-	-	-	-	-	-
	150	-	-	-	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-	+	+	+
15	75	-	-	-	-	-	+	+	+	+	+	+
	50	-	-	-	-	-	+	+	+	+	+	+
	25	-	-	-	-	-	+	+	+	+	+	+
	15	-	-	-	-	+	+	+	+	+	+	+
	10	-	-	-	-	+	+	+	+	+	+	+
20	5	-	-	-	-	+	+	+	+	+	+	+
	0	-	-	-	+	+	+	+	+	+	+	+

With simultaneous use of MIT and IPBC, a synergy occurred. The calculation of the synergy index is shown in Table IV. According to it, the lowest synergy index (0.67) for *Saccharomyces cerevisiae* was at a mixture of 83.3% by weight MIT and 16.7% by weight IPBC.

Table IV
Calculation of the synergy index for *Saccharomyces cerevisiae* at an incubation time of 96 hours

	MIC at		Concentration		Q_a/Q_A	Q_b/Q_B	Synergy index		
	MIT concentration Q_a (ppm)	IPBC concentration Q_b (ppm)	Total concentration $MIT + IPBC$	$Q_a + Q_b$ (ppm)	MIT (% wt)	IPBC (% wt)	$Q_a/Q_A + Q_b/Q_B$		
5	0	10	10	10	0.0	100.0	0.00	1.00	1.00
10	5	7.5	12.5	17.5	40.0	60.0	0.03	0.75	0.78
15	10	7.5	17.5	30	57.1	42.9	0.07	0.75	0.82
20	25	5	30	83.3	16.7	83.3	0.17	0.50	0.67
25	50	5	55	90.9	9.1	90.9	0.33	0.50	0.83
30	75	4	79	94.9	5.1	94.9	0.50	0.40	0.90
35	100	2	102	98.0	2.0	98.0	0.67	0.20	0.87
40	150	0	150	100.0	0.0	100.0	1.00	0.00	1.00

Example 3

As in Example 1, the synergy of MIT and IPBC in relation to the microorganism *Candida valida* is demonstrated.

The test arrangements again included a Sabouraud maltose broth as culture medium. The cell density was 10^6 cells/ml. The incubation time was 96 hours at 25° C. Every sample was incubated at 120 r.p.m. on an incubation shaker.

Table V below shows the MIC values of the tested biocide compositions. The MIC value with the use of MIT alone was 75 ppm and 2.5 ppm with the use of IPBC alone.

Table V

MIC values for *Candida valida*
at an incubation time of 96 hours

MIT Concen- tration (ppm)	IPBC concentration (ppm)										
	7.5	5	2.5	2	1.5	1.25	1	0.75	0.5	0.25	0
300	-	-	-	-	-	-	-	-	-	-	-
250	-	-	-	-	-	-	-	-	-	-	-
200	-	-	-	-	-	-	-	-	-	-	-
150	-	-	-	-	-	-	-	-	-	-	-
100	-	-	-	-	-	-	-	-	-	-	-
75	-	-	-	-	-	-	-	-	-	-	-
50	-	-	-	-	-	-	+	+	+	+	+
25	-	-	-	-	-	-	+	+	+	+	+
15	-	-	-	-	-	+	+	+	+	+	+
10	-	-	-	-	-	+	+	+	+	+	+
5	-	-	-	+	+	+	+	+	+	+	+
0	-	-	-	+	+	+	+	+	+	+	+

With simultaneous use of MIT and IPBC, a synergy occurred. The calculation
of the synergy index is shown in Table VI. According to it, the lowest synergy index
(0.73) for *Candida valida* was at a mixture of 87.0% by weight MIT and 13% by weight
IPBC, as well as at a mixture of 96.2% by weight MIT and 3.8% by weight IPBC.

Table VI
Calculation of synergy for *Candida valida*
at an incubation time of 96 hours

	MIC at		Concentration		Q_a/Q_A	Q_b/Q_B	Synergy index
	MIT concentration Q_a (ppm)	IPBC concentration Q_b (ppm)	Total concentration MIT + IPBC $Q_a + Q_b$ (ppm)	MIT (% wt)	IPBC (% wt)		
5	0	2.5	2.5	0.0	100.0	0.00	1.00
10	10	2	12	83.3	16.7	0.13	0.80
15	10	1.5	11.5	87.0	13.0	0.13	0.60
15	15	1.5	16.5	90.9	9.1	0.20	0.60
20	25	1.5	26.5	94.3	5.7	0.33	0.60
20	25	1.25	26.25	95.2	4.8	0.33	0.50
20	25	1	26	96.2	3.8	0.33	0.40
20	75	0	75	100.0	0.0	1.00	0.00
							0.00 $Q_a/Q_A + Q_b/Q_B$

Example 4

As in Example 1, the synergy of the two active ingredients MIT and IPBC in relation to the microorganism *Aspergillus niger* is demonstrated.

30

The test arrangements again included a Sabouraud maltose broth as culture medium. The cell density was 10^6 cells/ml. The incubation time was 96 hours at 25° C. Every sample was incubated at 120 r.p.m. on an incubation shaker.

Table VII below shows the MIC values of the tested biocide compositions. The MIC value with the use of MIT alone was 750 ppm and with the use of IPBC alone 5 ppm.

Table VII

MIC values for *Aspergillus niger*
at an incubation time of 96 hours

	MIT Concen- tration (ppm)	IPBC concentration (ppm)										
		5	2.5	2	1.5	1.25	1	0.75	0.5	0.25	0.1	0
5	750	-	-	-	-	-	-	-	-	-	-	-
10	500	-	-	-	-	-	-	+	+	+	+	+
15	250	-	-	-	+	+	+	+	+	+	+	+
20	100	-	-	+	+	+	+	+	+	+	+	+
25	50	-	+	+	+	+	+	+	+	+	+	+
30	40	-	+	+	+	+	+	+	+	+	+	+
35	30	-	+	+	+	+	+	+	+	+	+	+
40	20	-	+	+	+	+	+	+	+	+	+	+
45	15	-	+	+	+	+	+	+	+	+	+	+
50	10	-	+	+	+	+	+	+	+	+	+	+
55	7.5	-	+	+	+	+	+	+	+	+	+	+
60	5	-	+	+	+	+	+	+	+	+	+	+
65	0	-	+	+	+	+	+	+	+	+	+	+

With simultaneous use of MIT and IPBC, a synergy occurred. The calculation of the synergy index is shown in Table VIII. According to it, the lowest synergy index (0.63) for *Aspergillus niger* was at a mixture of 97.6% by weight MIT and 2.4% by weight IPBC.

Table VIII
Calculation of the synergy index for *Aspergillus niger*
at an incubation time of 96 hours

	MIC at		Concentration	Q_x/Q_A	Q_y/Q_B	Synergy index	
	MIT concentration Q_x (ppm)	IPBC concentration Q_y (ppm)					
10	Total concentration MIT + IPBC $Q_x + Q_y$ (ppm)						
	MIT (%) wt	IPBC (%) wt				$Q_x/Q_A + Q_y/Q_B$	
	0	5	5	0.0	100.0	0.00	1.00
	100	2.5	102.5	97.6	2.4	0.13	0.50
	250	2.5	252.5	99.0	1.0	0.33	0.50
	250	2	252	99.2	0.8	0.33	0.40
	500	1.5	501.5	99.7	0.3	0.67	0.30
15	500	1.25	501.25	99.8	0.2	0.67	0.25
	500	1	501	99.8	0.2	0.67	0.20
20	750	0	750	100.0	0.0	1.00	0.00
							1.00

Example 5

25 As in Example 1, the synergy of the two active ingredients MIT and IPBC in relation to the microorganism *Penicillium fumiculosum* is demonstrated.

The test arrangement again included a Sabouraud maltose broth as culture medium. The cell density was 10^6 germs/ml. The incubation time was 72 hours at 25° C. Every sample was incubated at 120 r.p.m. on an incubation shaker.

Table IX below shows the MIC values of the tested biocide compositions. The MIC value with the use of MIT alone was 200 ppm and with the use of IPBC alone 1.5 ppm.

Table IX
MIC values for *Penicillium funiculosum*
at an incubation time of 72 hours

	MIT Concen- tration (ppm)	IPBC concentration (ppm)										
		5	2.5	2	1.5	1.25	1	0.75	0.5	0.25	0.1	0
5	200	-	-	-	-	-	-	-	-	-	-	-
10	150	-	-	-	-	-	-	-	-	+	+	+
15	100	-	-	-	-	-	-	-	+	+	+	+
20	75	-	-	-	-	-	-	-	+	+	+	+
25	50	-	-	-	-	-	-	+	+	+	+	+
30	40	-	-	-	-	-	-	+	+	+	+	+
35	30	-	-	-	-	-	-	+	+	+	+	+
40	20	-	-	-	-	-	+	+	+	+	+	+
45	15	-	-	-	-	-	+	+	+	+	+	+
50	10	-	-	-	-	-	+	+	+	+	+	+
55	5	-	-	-	-	+	+	+	+	+	+	+
60	0	-	-	-	-	+	+	+	+	+	+	+

With simultaneous use of MIT and IPBC, a synergy occurred. The calculation of the synergy index is contained in Table X. According to it, the lowest synergy index (0.71) for *Penicillium funiculosum* was at a mixture of 99.3% by weight MIT and 0.7% by weight IPBC.

Table X

Calculation of the synergy index for *Penicillium funiculosum*
at an incubation time of 72 hours

	MIC at		Concentration		Q_s/Q_A	Q_s/Q_B	Synergy index
	MIT concentration Q_a (ppm)	IPBC concentration Q_b (ppm)	Total concentration MIT + IPBC $Q_a + Q_b$ (ppm)	MIT (% wt)	IPBC (% wt)		$Q_s/Q_A + Q_s/Q_B$
5	0	1.5	1.5	0.0	100.0	0.00	1.00
10	10	1.25	11.25	88.9	11.1	0.05	0.83
15	15	1.25	16.25	92.3	7.7	0.08	0.83
20	20	1.25	21.25	94.1	5.9	0.10	0.83
25	30	1	31	96.8	3.2	0.15	0.67
30	40	1	41	97.6	2.4	0.20	0.67
35	50	1	51	98.0	2.0	0.25	0.67
40	75	0.75	75.75	99.0	1.0	0.38	0.50
45	75	0.5	75.5	99.3	0.7	0.38	0.33
50	150	0.25	150.25	99.8	0.2	0.75	0.17
55	200	0	200	100.0	0.0	1.00	0.00
60							1.00

25

Example 6

Example 5 was repeated with the change that the incubation time was 96 hours instead of 72 hours.

30

Table XI below shows the MIC values of the tested biocide compositions. The MIC value with the use of MIT alone was 200 ppm and with the use of IPBC alone 1.5 ppm.

Table XI
MIC values for *Penicillium funiculosum*
at an incubation time of 96 hours

5	MIT Concen- tra-tion (ppm)	IPBC concentration (ppm)										
		5	2.5	2	1.5	1.25	1	0.75	0.5	0.25	0.1	0
10	200	-	-	-	-	-	-	-	-	-	-	-
	150	-	-	-	-	-	-	-	-	-	+	+
	100	-	-	-	-	-	-	-	-	+	+	+
	75	-	-	-	-	-	-	-	-	+	+	+
15	50	-	-	-	-	-	-	+	+	+	+	+
	40	-	-	-	-	-	-	+	+	+	+	+
	30	-	-	-	-	+	+	+	+	+	+	+
	20	-	-	-	-	+	+	+	+	+	+	+
	15	-	-	-	-	+	+	+	+	+	+	+
20	10	-	-	-	-	+	+	+	+	+	+	+
	5	-	-	-	-	+	+	+	+	+	+	+
	0	-	-	-	-	+	+	+	+	+	+	+

With simultaneous use of MIT and IPBC, a synergy occurred. The calculation of the synergy index is contained in Table XII. According to it, the lowest synergy index (0.71) for *Penicillium funiculosum* was at a mixture of 99.3% by weight MIT and 0.7% by weight IPBC.

Table XII

Calculation of the synergy index for *Penicillium funiculosum*
at an incubation time of 96 hours

5	MIC at		Total concentration MIT + IPBC $Q_a + Q_b$ (ppm)	Concentration		Q_a/Q_A	Q_b/Q_B	Synergy index $Q_a/Q_A + Q_b/Q_B$
	MIT concen- tration Q_a (ppm)	IPBC concen- tration Q_b (ppm)		MIT (% wt)	IPBC (% wt)			
10	0	1.5	1.5	0.0	100.0	0.00	1.00	1.00
	40	1	41	97.6	2.4	0.20	0.67	0.87
15	50	1	51	98.0	2.0	0.25	0.67	0.92
	75	0.75	75.75	99.0	1.0	0.38	0.50	0.88
	75	0.5	75.5	99.3	0.7	0.38	0.33	0.71
	150	0.25	150.25	99.8	0.2	0.75	0.17	0.92
20	200	0	200	100.0	0.0	1.00	0.00	1.00

March 1, 2000

APP

Claims

1. Biocide composition as an additive to substances susceptible to infestation by harmful organisms, containing 2-methylisothiazolin-3-one as a biocidal agent, characterized in that the biocide composition contains 3-iodo-2-propynyl-N-butylcarbamate as a further biocidal agent, with the exception of biocide compositions containing 5-chloro-2-methylisothiazolin-3-one.
5
2. Biocide composition according to claim 1, characterized in that it contains 2-methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate in a weight ratio of (100-1) : (1-50).
10
3. Biocide composition according to claim 2, characterized in that it contains 2-methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate in a weight ratio of (15-1) : (1-8).
15
4. Biocide composition according to any one of claims 1 through 3, characterized in that it contains 2-methylisothiazolin-3-one and 3-iodo-2-propynyl-N-butylcarbamate in a total concentration of 1 to 20% by weight, based on the total biocide composition.
20
5. Biocide composition according to any one of claims 1 through 4, characterized in that it contains a polar and/or a nonpolar liquid medium.
25
6. Biocide composition according to claim 5, characterized in that it contains as polar liquid medium water, an aliphatic alcohol having 1 to 4 carbon atoms, a glycol, a glycol ether, a glycol ester, a polyethylene glycol, a polypropylene glycol, N,N-dimethylformamide, 2,2,4-trimethylpentanedioilmonoisobutyrate, or a mixture of such substances.
30
7. Biocide composition according to claim 6, characterized in that the polar liquid medium is water and the composition has a pH value of 6 to 8.

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8. Use of a biocide composition according to any one of claims 1 through 7 for combatting harmful microorganisms.

Abstract

A biocide composition is disclosed as an additive to substances susceptible to infestation by harmful organisms, containing 2-methylisothiazolin-3-one as a biocidal agent. The composition is characterized in that it contains 3-iodo-2-propynyl-N-butylcarbamate as a further biocidal agent. In comparison to its individual constituents, the composition provided by the invention presents a synergistic biocidal action.

Docket No: 788-027APPLICATION FOR UNITED STATES LETTERS PATENT
DECLARATION, POWER OF ATTORNEY, AND PETITION

As a below-named inventor, I declare that:

My residence, post office address and citizenship are as stated next to my name; I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the invention which is described and which is claimed in the specification, entitled: SYNERGISTIC BIOCIDE COMPOSITION

The specification [] is attached hereto was filed on April 3, 2000, as Application Serial No. 09/509,932.

I hereby state that I have reviewed and understand the contents of said specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

COUNTRY	APPLICATION NUMBER	DATE (Day, Month, Year)	PRIORITY CLAIMED UNDER 35 U.S.C. 119
EP	98115723.3	20 August 1998	Yes <input checked="" type="checkbox"/> No []
PCT	PCTEP99/06056	18 August 1999	Yes <input checked="" type="checkbox"/> No []

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

¹In Non-Convention cases, a listing of all filings and current status of cases filed more than a year before the U.S. filing is required to comply with 37 CFR 1.56(a). Such a listing may be attached.

-2-

APPLICATION SERIAL NO.	FILING DATE	STATUS

I hereby appoint my attorneys with full power of substitution and revocation, to prosecute this application and to transact all business in the U.S. Patent & Trademark Office connected therewith:

Edward A. Hedman, Reg. No. 22,120; Thomas M. Gibson, Reg. No. 24,638; James V. Costigan, Reg. No. 25,669; Kenneth F. Florek, Reg. No. 33,173; Alan B. Clement, Reg. No. 34,583; and Martin P. Endres, Reg. No. 35,498.

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The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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